

SEQUENCE LISTING

<110> CURIS INC. AND WASHINGTON UNIVERSITY

<120> CONJOINT ADMINISTRATION OF MORPHOGENS AND ACE INHIBITORS IN TREATMENT OF CHRONIC RENAL FAILURE

<130> JJJ-P01-599

<140> 10/650,326

<141> 2003-08-28

<150> 60/406,431

<151> 2002-08-28

<160> 31

<170> PatentIn version 3.2

<210> 1

<211> 139

<212> PRT

<213> Homo sapiens

<400> 1

Ser Thr Gly Ser Lys Gln Arg Ser Gln Asn Arg Ser Lys Thr Pro Lys 1 5 10 15

Asn Gln Glu Ala Leu Arg Met Ala Asn Val Ala Glu Asn Ser Ser Ser 20 25 30

Asp Gln Arg Gln Ala Cys Lys His Glu Leu Tyr Val Ser Phe Arg 35 40 45

Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala Pro Glu Gly Tyr Ala Ala 50 55 60

Tyr Tyr Cys Glu Gly Glu Cys Ala Phe Pro Leu Asn Ser Tyr Met Asn 65 70 75 80

Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His Phe Ile Asn Pro 85 90 95

Glu Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln Leu Asn Ala Ile 100 105 110

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<211> 97

<212> PRT

<213> Homo sapiens

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His Arg Arg Leu Arg Ser Gln Glu Arg Arg Glu Met Gln Arg Glu Ile
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Leu Ser Ile Leu Gly Leu Pro His Arg Pro Arg Pro His Leu Gln Gly 20 25 30

Lys His Asn Ser Ala Pro Met Phe Met Leu Asp Leu Tyr Asn Ala Met 35 40 45

Ala Val Glu Glu Gly Gly Gly Pro Gly Gly Gln Gly Phe Ser Tyr Pro 50 55 60

Tyr Lys Ala Val Phe Ser Thr Gln Gly Pro Pro Leu Ala Ser Leu Gln 65 70 75 80

Asp Ser His Phe Leu Thr Asp Ala Asp Met Val Met Ser Phe Val Asn 85 90 95

Leu

<210> 3

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<212> PRT

<213> Homo sapiens

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Leu Trp Ala Pro Leu Phe Leu Leu Arg Ser Ala Leu Ala Asp Phe Ser 20 25 30

Leu Asp Asn Glu Val His Ser Ser Phe Ile His Arg Arg Leu Arg Ser 35 40 45

- Gln Glu Arg Arg Glu Met Gln Arg Glu Ile Leu Ser Ile Leu Gly Leu 50 60
- Pro His Arg Pro Arg Pro His Leu Gln Gly Lys His Asn Ser Ala Pro 65 70 75 80
- Met Phe Met Leu Asp Leu Tyr Asn Ala Met Ala Val Glu Glu Gly Gly 85 90 95
- Gly Pro Gly Gln Gly Phe Ser Tyr Pro Tyr Lys Ala Val Phe Ser 100 105 110
- Thr Gln Gly Pro Pro Leu Ala Ser Leu Gln Asp Ser His Phe Leu Thr 115 120 125
- Asp Ala Asp Met Val Met Ser Phe Val Asn Leu Val Glu His Asp Lys 130 135 140
- Glu Phe Phe His Pro Arg Tyr His His Arg Glu Phe Arg Phe Asp Leu 145 150 155 160
- Ser Lys Ile Pro Glu Gly Glu Ala Val Thr Ala Ala Glu Phe Arg Ile 165 170 175
- Tyr Lys Asp Tyr Ile Arg Glu Arg Phe Asp Asn Glu Thr Phe Arg Ile 180 185 190
- Ser Val Tyr Gln Val Leu Gln Glu His Leu Gly Arg Glu Ser Asp Leu 195 200 205
- Phe Leu Leu Asp Ser Arg Thr Leu Trp Ala Ser Glu Glu Gly Trp Leu 210 215 220
- Val Phe Asp Ile Thr Ala Thr Ser Asn His Trp Val Val Asn Pro Arg 225 230 235 240
- His Asn Leu Gly Leu Gln Leu Ser Val Glu Thr Leu Asp Gly Gln Ser 245 250 255
- Ile Asn Pro Lys Leu Ala Gly Leu Ile Gly Arg His Gly Pro Gln Asn 260 265 270

Lys Gln Pro Phe Met Val Ala Phe Phe Lys Ala Thr Glu Val His Phe 275 280 285

Arg Ser Ile Arg Ser Thr Gly Ser Lys Gln Arg Ser Gln Asn Arg Ser 290 295 300

Lys Thr Pro Lys Asn Gln Glu Ala Leu Arg Met Ala Asn Val Ala Glu 305 310 315 320

Asn Ser Ser Ser Asp Gln Arg Gln Ala Cys Lys Lys His Glu Leu Tyr 325 330 335

Val Ser Phe Arg Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala Pro Glu 340 345 350

Gly Tyr Ala Ala Tyr Tyr Cys Glu Gly Glu Cys Ala Phe Pro Leu Asn 355 360 365

Ser Tyr Met Asn Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His 370 380

Phe Ile Asn Pro Glu Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln 385 390 395

Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp Ser Ser Asn Val Ile 405 410 415

Leu Lys Lys Tyr Arg Asn Met Val Val Arg Ala Cys Gly Cys His 420 425 430

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<212> PRT

<213> Mus musculus

<400> 4

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Asn Gln Glu Ala Leu Arg Met Ala Ser Val Ala Glu Asn Ser Ser Ser 20 25 30

Asp Gln Arg Gln Ala Cys Lys His Glu Leu Tyr Val Ser Phe Arg 35 40 45

Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala Pro Glu Gly Tyr Ala Ala 50 60

Tyr Tyr Cys Glu Gly Glu Cys Ala Phe Pro Leu Asn Ser Tyr Met Asn 65 70 75 80

Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His Phe Ile Asn Pro 85 90 95

Asp Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln Leu Asn Ala Ile 100 105 110

Ser Val Leu Tyr Phe Asp Asp Ser Ser Asn Val Ile Leu Lys Lys Tyr 115 120 125

Arg Asn Met Val Val Arg Ala Cys Gly Cys His 130 135

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<212> PRT

<213> Homo sapiens

<400> 5

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Pro Gln Ala Asn Arg Leu Pro Gly Ile Phe Asp Asp Val His Gly Ser 20 25 30

His Gly Arg Gln Val Cys Arg Arg His Glu Leu Tyr Val Ser Phe Gln 35 40 45

Asp Leu Gly Trp Leu Asp Trp Val Ile Ala Pro Gln Gly Tyr Ser Ala 50 55 60

Tyr Tyr Cys Glu Gly Glu Cys Ser Phe Pro Leu Asp Ser Cys Met Asn 65 70 75 80

Ala Thr Asn His Ala Ile Leu Gln Ser Leu Val His Leu Met Lys Pro 85 90 95 Asn Ala Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr 100 105 110

Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His 115 120 125

Arg Asn Met Val Val Lys Ala Cys Gly Cys His 130 135

<210> 6

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<212> PRT

<213> Mus musculus

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Pro His Pro Asn Lys Leu Pro Gly Ile Phe Asp Asp Gly His Gly Ser 20 25 30

Arg Gly Arg Glu Val Cys Arg Arg His Glu Leu Tyr Val Ser Phe Arg 35 40 45

Asp Leu Gly Trp Leu Asp Trp Val Ile Ala Pro Gln Gly Tyr Ser Ala 50 60

Tyr Tyr Cys Glu Gly Glu Cys Ala Phe Pro Leu Asp Ser Cys Met Asn 65 70 75 80

Ala Thr Asn His Ala Ile Leu Gln Ser Leu Val His Leu Met Lys Pro $85 \hspace{1cm} 90 \hspace{1cm} 95$

Asp Val Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr

Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His 115 120 125

Arg Asn Met Val Val Lys Ala Cys Gly Cys His 130 135

<210> 7 <211> 588 <212> PRT

<213> Drosophila melanogaster

<400> 7

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Ile Val Arg Val Ala Ser Thr Glu Asp Ile Ser Gln Arg Phe Ile Ala 20 25 30

Ala Ile Ala Pro Val Ala Ala His Ile Pro Leu Ala Ser Ala Ser Gly 35 40 45

Ser Gly Ser Gly Arg Ser Gly Ser Arg Ser Gly Gly Ala Ser Thr Ser 50 55 60

Thr Ala Leu Ala Lys Ala Phe Asn Pro Phe Ser Glu Pro Ala Ser Phe 65 70 75 80

Ser Asp Ser Asp Lys Ser His Arg Ser Lys Thr Asn Lys Lys Pro Ser 85 90 95

Lys Ser Asp Ala Asn Arg Gln Phe Asn Glu Val His Lys Pro Arg Thr 100 105 110

Asp Gln Leu Glu Asn Ser Lys Asn Met Ser Lys Gln Leu Val Asn Lys 115 120 125

Pro Asn His Asn Lys Met Ala Val Lys Glu Gln Arg Ser His His Lys 130 135 140

Lys Ser His His Arg Ser His Gln Pro Lys Gln Ala Ser Ala Ser 145 150 155 160

Thr Glu Ser His Gln Ser Ser Ser Ile Glu Ser Ile Phe Val Glu Glu 165 170 175

Pro Thr Leu Val Leu Asp Arg Glu Val Ala Ser Ile Asn Val Pro Ala 180 185 190

Asn Ala Lys Ala Ile Ile Ala Glu Gln Gly Pro Ser Thr Tyr Ser Lys 195 200 205

(Glu	Ala 210	Leu	Ile	Lys	Asp	Lys 215	Leu	Lys	Pro	Asp	Pro 220	Ser	Thr	Leu	Val
	Glu 225	Ile	Glu	Lys	Ser	Leu 230	Leu	Ser	Leu	Phe	Asn 235	Met	Lys	Arg	Pro	Pro 240
-	Lys	Ile	Asp	Arg	Ser 245	Lys	Ile	Ile	Ile	Pro 250	Glu	Pro	Met	Lys	Lys 255	Leu
•	Гуr	Ala	Glu	Ile 260	Met	Gly	His	Glu	Leu 265	Asp	Ser	Val	Asn	Ile 270	Pro	Lys
]	Pro	Gly	Leu 275	Leu	Thr	Lys	Ser	Ala 280	Asn	Thr	Val	Arg	Ser 285	Phe	Thr	His
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	Leu 305	His	Phe	Asp	Val	Lys 310	Ser	Ile	Pro	Ala	Asp 315	Glu	Lys	Leu	Lys	Ala 320
1	Ala	Glu	Leu	Gln	Leu 325	Thr	Arg	Asp	Ala	Leu 330	Ser	Gln	Gln	Val	Val 335	Ala
:	Ser	Arg	Ser	Ser 340	Ala	Asn	Arg	Thr	Arg 345	Tyr	Gln	Val	Leu	Val 350	Tyr	Asp
	Ile	Thr	Arg 355	Val	Gly	Val	Arg	Gly 360	Gln	Arg	Glu	Pro	Ser 365	Tyr	Leu	Leu
]	Leu	Asp 370	Thr	Lys	Thr	Val	Arg 375	Leu	Asn	Ser	Thr	Asp 380	Thr	Val	Ser	Leu
	Asp 385	Val	Gln	Pro	Ala	Val 390	Asp	Arg	Trp	Leu	Ala 395	Ser	Pro	Gln	Arg	Asn 400
-	Гуr	Gly	Leu	Leu	Val 405	Glu	Val	Arg	Thr	Val 410	Arg	Ser	Leu	Lys	Pro 415	Ala
I	Pro	His	His	His 420	Val	Arg	Leu	Arg	Arg 425	Ser	Ala	Asp	Glu	Ala 430	His	Glu
7	Arg	Trp	Gln	His	Lys	Gln	Pro	Leu	Leu	Phe	Thr	Tyr	Thr	Asp	Asp	Gly

435 440 445

Arg His Lys Ala Arg Ser Ile Arg Asp Val Ser Gly Gly Glu Gly Gly 450 455 460

Gly Lys Gly Gly Arg Asn Lys Arg Gln Pro Arg Arg Pro Thr Arg Arg
465 470 475 480

Lys Asn His Asp Asp Thr Cys Arg Arg His Ser Leu Tyr Val Asp Phe 485 490 495

Ser Asp Val Gly Trp Asp Asp Trp Ile Val Ala Pro Leu Gly Tyr Asp 500 505 510

Ala Tyr Tyr Cys His Gly Lys Cys Pro Phe Pro Leu Ala Asp His Phe 515 520 525

Asn Ser Thr Asn His Ala Val Val Gln Thr Leu Val Asn Asn Met Asn 530 540

Pro Gly Lys Val Pro Lys Ala Cys Cys Val Pro Thr Gln Leu Asp Ser 545 550 555 560

Val Ala Met Leu Tyr Leu Asn Asp Gln Ser Thr Val Val Leu Lys Asn 565 570 575

Tyr Gln Glu Met Thr Val Val Gly Cys Gly Cys Arg 580 585

<210> 8

<211> 360

<212> PRT

<213> Xenopus laevis

<400> 8

Met Val Trp Leu Arg Leu Trp Ala Phe Leu His Ile Leu Ala Ile Val 1 5 10 15

Thr Leu Asp Pro Glu Leu Lys Arg Arg Glu Glu Leu Phe Leu Arg Ser 20 25 30

Leu Gly Phe Ser Ser Lys Pro Asn Pro Val Ser Pro Pro Pro Val Pro
35 40 45

Lys Lys Pro Asp Leu Cys Phe Val Glu Phe Asn Val Pro Gly Ser Val Ile Arg Val Phe Pro Asp Gln Gly Arg Phe Ile Ile Pro Tyr Ser Asp Asp Ile His Pro Thr Gln Cys Leu Glu Lys Arg Leu Phe Phe Asn Ile Ser Ala Ile Glu Lys Glu Glu Arg Val Thr Met Gly Ser Gly Ile Glu Val Gln Pro Glu His Leu Leu Arg Lys Gly Ile Asp Leu Arg Leu Tyr Arg Thr Leu Gln Ile Thr Leu Lys Gly Met Gly Arg Ser Lys Thr Ser Arg Lys Leu Leu Val Ala Gln Thr Phe Arg Leu Leu His Lys Ser Leu Phe Phe Asn Leu Thr Glu Ile Cys Gln Ser Trp Gln Asp Pro Leu Lys Asn Leu Gly Leu Val Leu Glu Ile Phe Pro Lys Lys Glu Ser Ser Trp Met Ser Thr Ala Asn Asp Glu Cys Lys Asp Ile Gln Thr Phe Leu Tyr Thr Ser Leu Leu Thr Val Thr Leu Asn Pro Leu Arg Cys Lys Arg Pro Arg Arg Lys Arg Ser Tyr Ser Lys Leu Pro Phe Thr Ala Ser

Asn Ile Cys Lys Lys Arg His Leu Tyr Val Glu Phe Lys Asp Val Gly

Ser Ile Leu Trp Arg Ile Phe Asn Gln Arg Met Gly Ser Ser Ile Gln

Trp Gln Asn Trp Val Ile Ala Pro Gln Gly Tyr Met Ala Asn Tyr Cys 275 280 285

Tyr Gly Glu Cys Pro Tyr Pro Leu Thr Glu Ile Leu Asn Gly Ser Asn 290 295 300

His Ala Ile Leu Gln Thr Leu Val His Ser Ile Glu Pro Glu Asp Ile 305 310 315 320

Pro Leu Pro Cys Cys Val Pro Thr Lys Met Ser Pro Ile Ser Met Leu 325 330 335

Phe Tyr Asp Asn Asn Asp Asn Val Val Leu Arg His Tyr Glu Asn Met 340 345 350

Ala Val Asp Glu Cys Gly Cys Arg 355 360

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<213> Mus musculus

<400> 9

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Pro Pro Gln Gln Gln Gln Gln Gln Gln Gln Gln Thr Ala Arg Glu 35 40 45

Glu Pro Pro Pro Gly Arg Leu Lys Ser Ala Pro Leu Phe Met Leu Asp 50 55 60

Leu Tyr Asn Ala Leu Ser Asn Asp Asp Glu Glu Asp Gly Ala Ser Glu 65 70 75 80

Gly Val Gly Gln Glu Pro Gly Ser His Gly Gly Ala Ser Ser Gln
85 90 95

Leu Arg Gln Pro Ser Pro Gly Ala Ala His Ser Leu Asn Arg Lys Ser 100 105 110

Leu	Leu	Ala 115	Pro	Gly	Pro	Gly	Gly 120	Gly	Ala	Ser	Pro	Leu 125	Thr	Ser	Ala
Gln	Asp 130	Ser	Ala	Phe	Leu	Asn 135	Asp	Ala	Asp	Met	Val 140	Met	Ser	Phe	Val
Asn 145	Leu	Val	Glu	Tyr	Asp 150	Lys	Glu	Phe	Ser	Pro 155	His	Gln	Arg	His	His 160
Lys	Glu	Phe	Lys	Phe 165	Asn	Leu	Ser	Gln	Ile 170	Pro	Glu	Gly	Glu	Ala 175	Val
Thr	Ala	Ala	Glu 180	Phe	Arg	Val	Tyr	Lys 185	Asp	Cys	Val	Val	Gly 190	Ser	Phe
Lys	Asn	Gln 195	Thr	Phe	Leu	Ile	Ser 200	Ile	Tyr	Gln	Val	Leu 205	Gln	Glu	His
Gln	His 210	Arg	Asp	Ser	Asp	Leu 215	Phe	Leu	Leu	Asp	Thr 220	Arg	Val	Val	Trp
Ala 225	Ser	Glu	Glu	Gly	Trp 230	Leu	Glu	Phe	Asp	Ile 235	Thr	Ala	Thr	Ser	Asn 240
Leu	Trp	Val	Val	Thr 245	Pro	Gln	His	Asn	Met 250	Gly	Leu	Gln	Leu	Ser 255	Val
Val	Thr	Arg	Asp 260	Gly	Leu	His	Val	Asn 265	Pro	Arg	Ala	Ala	Gly 270	Leu	Val
Gly	Arg	Asp 275	Gly	Pro	Tyr	Asp	Lys 280	Gln	Pro	Phe	Met	Val 285	Ala	Phe	Phe
Lys	Val 290	Ser	Glu	Val	His	Val 295	Arg	Thr	Thr	Arg	Ser 300	Ala	Ser	Ser	Arg
Arg 305	Arg	Gln	Gln	Ser	Arg 310	Asn	Arg	Ser	Thr	Gln 315	Ser	Gln	Asp	Val	Ser 320
Arg	Gly	Ser	Gly	Ser	Ser	Asp	Tyr	Asn	Gly	Ser	Glu	Leu	Lys	Thr	Ala

Cys Lys Lys His Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Gln 340 345 350

Asp Trp Ile Ile Ala Pro Lys Gly Tyr Ala Ala Asn Tyr Cys Asp Gly 355 360 365

Glu Cys Ser Phe Pro Leu Asn Ala His Met Asn Ala Thr Asn His Ala $370 \hspace{1.5cm} 375 \hspace{1.5cm} 380$

Ile Val Gln Thr Leu Val His Leu Met Asn Pro Glu Tyr Val Pro Lys 385 390 395 400

Pro Cys Cys Ala Pro Thr Lys Leu Asn Ala Ile Ser Val Leu Tyr Phe 405 410 415

Asp Asp Asn Ser Asn Val Ile Leu Lys Lys Tyr Arg Asn Met Val Val 420 425 430

Arg Ala Cys Gly Cys His 435

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<212> DNA

<213> Homo sapiens

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tctttaattt aagttctatc	cccacggagg	agtttatcac	ctcagcagag	cttcaggttt	780
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atgaacacag ctggtcacag	ataaggccat	tgctagtaac	ttttggccat	gatggaaaag	1140
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tggctgatca tctgaactcc	actaatcatg	ccattgttca	gacgttggtc	aactctgtta	1380
actctaagat tcctaaggca	tgctgtgtcc	cgacagaact	cagtgctatc	tcgatgctgt	1440
accttgacga gaatgaaaag	gttgtattaa	agaactatca	ggacatggtt	gtggagggtt	1500
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<212> DNA

<213> Homo sapiens

<400> 11

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cccggccagc	cgggccaaca	ccgtgaggag	cttccaccac	gaagaacatc	tggagaacat	7 80
cccagggacc	agtgaaaact	ctgcttttcg	tttcctcttt	aacctcagca	gcatccctga	840
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tgattgggaa	aggggcttcc	accgtataaa	catttatgag	gttatgaagc	ccccagcaga	960
agtggtgcct	gggcacctca	tcacacgact	actggacacg	agactggtcc	accacaatgt	1020
gacacggtgg	gaaacttttg	atgtgagccc	tgcggtcctt	cgctggaccc	gggagaagca	1080
gccaaactat	gggctagcca	ttgaggtgac	tcacctccat	cagactcgga	cccaccaggg	1140
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caactcaacc	aaccatgcca	ttgtgcagac	cctggtcaat	tctgtcaatt	ccagtatccc	1500
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<210> 12

<211> 472

<212> PRT

<213> Homo sapiens

<400> 12

Met Ala Gly Ala Ser Arg Leu Leu Phe Leu Trp Leu Gly Cys Phe Cys 1 5 10 15

Val Ser Leu Ala Gln Gly Glu Arg Pro Lys Pro Pro Phe Pro Glu Leu 20 25 30

Arg Lys Ala Val Pro Gly Asp Arg Thr Ala Gly Gly Pro Asp Ser

- Glu Leu Gln Pro Gln Asp Lys Val Ser Glu His Met Leu Arg Leu Tyr 50 55 60
- Asp Arg Tyr Ser Thr Val Gln Ala Ala Arg Thr Pro Gly Ser Leu Glu 65 70 75 80
- Gly Gly Ser Gln Pro Trp Arg Pro Arg Leu Leu Arg Glu Gly Asn Thr 85 90 95
- Val Arg Ser Phe Arg Ala Ala Ala Glu Thr Leu Glu Arg Lys Gly
 100 105 110
- Leu Tyr Ile Phe Asn Leu Thr Ser Leu Thr Lys Ser Glu Asn Ile Leu 115 120 125
- Ser Ala Thr Leu Tyr Phe Cys Ile Gly Glu Leu Gly Asn Ile Ser Leu 130 135 140
- Ser Cys Pro Val Ser Gly Gly Cys Ser His His Ala Gln Arg Lys His 145 150 155 160
- Ile Gln Ile Asp Leu Ser Ala Trp Thr Leu Lys Phe Ser Arg Asn Gln 165 170 175
- Ser Gln Leu Leu Gly His Leu Ser Val Asp Met Ala Lys Ser His Arg 180 185 190
- Asp Ile Met Ser Trp Leu Ser Lys Asp Ile Thr Gln Phe Leu Arg Lys 195 200 205
- Ala Lys Glu Asn Glu Glu Phe Leu Ile Gly Phe Asn Ile Thr Ser Lys 210 215 220
- Gly Arg Gln Leu Pro Lys Arg Arg Leu Pro Phe Pro Glu Pro Tyr Ile 225 230 235 240
- Leu Val Tyr Ala Asn Asp Ala Ala Ile Ser Glu Pro Glu Ser Val Val 245 250 255
- Ser Ser Leu Gln Gly His Arg Asn Phe Pro Thr Gly Thr Val Pro Lys 260 265 270

Trp Asp Ser His Ile Arg Ala Ala Leu Ser Ile Glu Arg Arg Lys Lys 275 280 285

Arg Ser Thr Gly Val Leu Leu Pro Leu Gln Asn Asn Glu Leu Pro Gly 290 295 300

Ala Glu Tyr Gln Tyr Lys Lys Asp Glu Val Trp Glu Glu Arg Lys Pro 305 310 315 320

Tyr Lys Thr Leu Gln Ala Gln Ala Pro Glu Lys Ser Lys Asn Lys Lys 325 330 335

Lys Gln Arg Lys Gly Pro His Arg Lys Ser Gln Thr Leu Gln Phe Asp 340 345 350

Glu Gln Thr Leu Lys Lys Ala Arg Arg Lys Gln Trp Ile Glu Pro Arg 355 360 365

Asn Cys Ala Arg Arg Tyr Leu Lys Val Asp Phe Ala Asp Ile Gly Trp $370 \hspace{1cm} 375 \hspace{1cm} 380$

Ser Glu Trp Ile Ile Ser Pro Lys Ser Phe Asp Ala Tyr Tyr Cys Ser 385 390 395 400

Gly Ala Cys Gln Phe Pro Met Pro Lys Ser Leu Lys Pro Ser Asn His 405 410 415

Ala Thr Ile Gln Ser Ile Val Arg Ala Val Gly Val Val Pro Gly Ile 420 425 430

Pro Glu Pro Cys Cys Val Pro Glu Lys Met Ser Ser Leu Ser Ile Leu 435 440 445

Phe Phe Asp Glu Asn Lys Asn Val Val Leu Lys Val Tyr Pro Asn Met 450 455 460

Thr Val Glu Ser Cys Ala Cys Arg 465 470

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<213> Homo sapiens

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Pro Gly Pro Ala Ala Ala Leu Leu Gln Ala Leu Gly Leu Arg Asp Glu 35 40 45

Pro Gln Gly Ala Pro Arg Leu Arg Pro Val Pro Pro Val Met Trp Arg 50 55 60

Leu Phe Arg Arg Arg Asp Pro Gln Glu Thr Arg Ser Gly Ser Arg Arg 65 70 75 80

Thr Ser Pro Gly Val Thr Leu Gln Pro Cys His Val Glu Glu Leu Gly 85 90 95

Val Ala Gly Asn Ile Val Arg His Ile Pro Asp Arg Gly Ala Pro Thr 100 105 110

Arg Ala Ser Glu Pro Val Ser Ala Ala Gly His Cys Pro Glu Trp Thr 115 120 125

Val Val Phe Asp Leu Ser Ala Val Glu Pro Ala Glu Arg Pro Ser Arg 130 135 140

Ala Arg Leu Glu Leu Arg Phe Ala Ala Ala Ala Ala Ala Ala Pro Glu 145 150 155 160

Gly Gly Trp Glu Leu Ser Val Ala Gln Ala Gly Gln Gly Ala Gly Ala 165 170 175

Asp Pro Gly Pro Val Leu Leu Arg Gln Leu Val Pro Ala Leu Gly Pro 180 185 190

Pro Val Arg Ala Glu Leu Leu Gly Ala Ala Trp Ala Arg Asn Ala Ser 195 200 205

Trp Pro Arg Ser Leu Arg Leu Ala Leu Ala Leu Arg Pro Arg Ala Pro

Ala Ala Cys Ala Arg Leu Ala Glu Ala Ser Leu Leu Leu Val Thr Leu 225 230 235 240

Asp Pro Arg Leu Cys His Pro Leu Ala Arg Pro Arg Arg Asp Ala Glu 245 250 255

Pro Val Leu Gly Gly Gly Pro Gly Gly Ala Cys Arg Ala Arg Arg Leu 260 265 270

Tyr Val Ser Phe Arg Glu Val Gly Trp His Arg Trp Val Ile Ala Pro 275 280 285

Arg Gly Phe Leu Ala Asn Tyr Cys Gln Gly Gln Cys Ala Leu Pro Val 290 295 300

Ala Leu Ser Gly Ser Gly Gly Pro Pro Ala Leu Asn His Ala Val Leu 305 310 315 320

Arg Ala Leu Met His Ala Ala Pro Gly Ala Ala Asp Leu Pro Cys 325 330 335

Cys Val Pro Ala Arg Leu Ser Pro Ile Ser Val Leu Phe Phe Asp Asn 340 345 350

Ser Asp Asn Val Val Leu Arg Gln Tyr Glu Asp Met Val Val Asp Glu 355 360 365

Cys Gly Cys Arg 370

<210> 14

<211> 455

<212> PRT

<213> Drosophila melanogaster

<400> 14

Met Ser Gly Leu Arg Asn Thr Ser Glu Ala Val Ala Val Leu Ala Ser 1 5 10 15

Leu Gly Leu Gly Met Val Leu Leu Met Phe Val Ala Thr Thr Pro Pro 20 25 30

Ala Val Glu Ala Thr Gln Ser Gly Ile Tyr Ile Asp Asn Gly Lys Asp Gln Thr Ile Met His Arg Val Leu Ser Glu Asp Asp Lys Leu Asp Val Ser Tyr Glu Ile Leu Glu Phe Leu Gly Ile Ala Glu Arg Pro Thr His Leu Ser Ser His Gln Leu Ser Leu Arg Lys Ser Ala Pro Lys Phe Leu Leu Asp Val Tyr His Arg Ile Thr Ala Glu Glu Gly Leu Ser Asp Gln Asp Glu Asp Asp Asp Tyr Glu Arg Gly His Arg Ser Arg Arg Ser Ala Asp Leu Glu Glu Asp Glu Gly Glu Gln Gln Lys Asn Phe Ile Thr Asp Leu Asp Lys Arg Ala Ile Asp Glu Ser Asp Ile Ile Met Thr Phe Leu Asn Lys Arg His His Asn Val Asp Glu Leu Arg His Glu His Gly Arg Arg Leu Trp Phe Asp Val Ser Asn Val Pro Asn Asp Asn Tyr Leu Val Met Ala Glu Leu Arg Ile Tyr Gln Asn Ala Asn Glu Gly Lys Trp Leu Thr Ala Asn Arg Glu Phe Thr Ile Thr Val Tyr Ala Ile Gly Thr Gly Thr Leu Gly Gln His Thr Met Glu Pro Leu Ser Ser Val Asn Thr Thr

Gly Asp Tyr Val Gly Trp Leu Glu Leu Asn Val Thr Glu Gly Leu His

Glu Trp Leu Val Lys Ser Lys Asp Asn His Gly Ile Tyr Ile Gly Ala 260 265 270

His Ala Val Asn Arg Pro Asp Arg Glu Val Lys Leu Asp Asp Ile Gly 275 280 285

Leu Ile His Arg Lys Val Asp Asp Glu Phe Gln Pro Phe Met Ile Gly 290 295 300

Phe Phe Arg Gly Pro Glu Leu Ile Lys Ala Thr Ala His Ser Ser His 305 310 315 320

His Arg Ser Lys Arg Ser Ala Ser His Pro Arg Lys Arg Lys Ser 325 330 335

Val Ser Pro Asn Asn Val Pro Leu Leu Glu Pro Met Glu Ser Thr Arg 340 345 350

Ser Cys Gln Met Gln Thr Leu Tyr Ile Asp Phe Lys Asp Leu Gly Trp 355 360 365

His Asp Trp Ile Ile Ala Pro Glu Gly Tyr Gly Ala Phe Tyr Cys Ser 370 380

Gly Glu Cys Asn Phe Pro Leu Asn Ala His Met Asn Ala Thr Asn His 385 390 395 400

Ala Ile Val Gln Thr Leu Val His Leu Leu Glu Pro Lys Lys Val Pro 405 410 415

Lys Pro Cys Cys Ala Pro Thr Arg Leu Gly Ala Leu Pro Val Leu Tyr 420 425 430

His Leu Asn Asp Glu Asn Val Asn Leu Lys Lys Tyr Arg Asn Met Ile 435 440 445

Val Lys Ser Cys Gly Cys His 450 455

<210> 15

<211> 454

<212> PRT

<213> Homo sapiens

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Ser Cys Trp Val Leu Val Gly Tyr Ala Lys Gly Gly Leu Gly Asp Asn 20 25 30

His Val His Ser Ser Phe Ile Tyr Arg Arg Leu Arg Asn His Glu Arg 35 40 45

Arg Glu Ile Gln Arg Glu Ile Leu Ser Ile Leu Gly Leu Pro His Arg 50 55 60

Pro Arg Pro Phe Ser Pro Gly Lys Gln Ala Ser Ser Ala Pro Leu Phe 65 70 75 80

Met Leu Asp Leu Tyr Asn Ala Met Thr Asn Glu Glu Asn Pro Glu Glu 85 90 95

Ser Glu Tyr Ser Val Arg Ala Ser Leu Ala Glu Glu Thr Arg Gly Ala 100 105 110

Arg Lys Gly Tyr Pro Ala Ser Pro Asn Gly Tyr Pro Arg Arg Ile Gln
115 120 125

Leu Ser Arg Thr Thr Pro Leu Thr Thr Gln Ser Pro Pro Leu Ala Ser 130 135 140

Leu His Asp Thr Asn Phe Leu Asn Asp Ala Asp Met Val Met Ser Phe 145 150 155 160

Val Asn Leu Val Glu Arg Asp Lys Asp Phe Ser His Gln Arg Arg His 165 170 175

Tyr Lys Glu Phe Arg Phe Asp Leu Thr Gln Ile Pro His Gly Glu Ala 180 185 190

Val Thr Ala Ala Glu Phe Arg Ile Tyr Lys Asp Arg Ser Asn Asn Arg 195 200 205

Phe Glu Asn Glu Thr Ile Lys Ile Ser Ile Tyr Gln Ile Ile Lys Glu 210 215 220

Tyr 1 225	ľhr	Asn	Arg	Asp	Ala 230	Asp	Leu	Phe	Leu	Leu 235	Asp	Thr	Arg	Lys	Ala 240
Gln A	Ala	Leu	Asp	Val 245	Gly	Trp	Leu	Val	Phe 250	Asp	Ile	Thr	Val	Thr 255	Ser
Asn H	lis	Trp	Val 260	Ile	Asn	Pro	Gln	Asn 265	Asn	Leu	Gly	Leu	Gln 270	Leu	Cys
Ala G	Glu	Thr 275	Gly	Asp	Gly	Arg	Ser 280	Ile	Asn	Val	Lys	Ser 285	Ala	Gly	Leu
Val G	Gly 290	Arg	Gln	Gly	Pro	Gln 295	Ser	Lys	Gln	Pro	Phe 300	Met	Val	Ala	Phe
Phe I 305	Буs	Ala	Ser	Glu	Val 310	Leu	Leu	Arg	Ser	Val 315	Arg	Ala	Ala	Asn	Lys 320
Arg I	Lys	Asn	Gln	Asn 325	Arg	Asn	Lys	Ser	Ser 330	Ser	His	Gln	Asp	Ser 335	Ser
Arg M	1et	Ser	Ser 340	Val	Gly	Asp	Tyr	Asn 345	Thr	Ser	Glu	Gln	Lys 350	Gln	Ala
Cys I	Lys	Lys 355	His	Glu	Leu	Tyr	Val 360	Ser	Phe	Arg	Asp	Leu 365	Gly	Trp	Gln
Asp T	Trp 370	Ile	Ile	Ala	Pro	Glu 375	Gly	Tyr	Ala	Ala	Phe 380	Tyr	Cys	Asp	Gly
Glu C 385	Cys	Ser	Phe	Pro	Leu 390	Asn	Ala	His	Met	Asn 395	Ala	Thr	Asn	His	Ala 400
Ile V	/al	Gln	Thr	Leu 405	Val	His	Leu	Met	Phe 410	Pro	Asp	His	Val	Pro 415	Lys
Pro C	Cys	Cys	Ala 420	Pro	Thr	Lys	Leu	Asn 425	Ala	Ile	Ser	Val	Leu 430	Tyr	Phe
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Gly Ala Ala His Pro Leu Asn Arg Lys Ser Leu Leu Ala Pro Gly Ser 180 185 190

Trp Pro His Glu Ala Ala Ser Ser Ser Gln Arg Arg Gln Pro Pro Pro

170

165

Gly	Ser	Gly 195	Gly	Ala	Ser	Leu 200	Thr	Ser	Ala	Gln	Asp 205	Ser	Ala	Phe

Leu Asn Asp Ala Asp Met Val Met Ser Phe Val Asn Leu Val Glu Tyr 210 215 220

Asp Lys Glu Phe Ser Pro Arg Gln Arg His His Lys Glu Phe Lys Phe 225 230 235 240

Asn Leu Ser Gln Ile Pro Glu Gly Glu Val Val Thr Ala Ala Glu Phe 245 250 255

Arg Ile Tyr Lys Asp Cys Val Met Gly Ser Phe Lys Asn Gln Thr Phe 260 265 270

Leu Ile Ser Ile Tyr Gln Val Leu Gln Glu His Gln His Arg Asp Ser 275 280 285

Asp Leu Phe Leu Leu Asp Thr Arg Val Val Trp Ala Ser Glu Glu Gly 290 295 300

Trp Leu Glu Phe Asp Ile Thr Ala Thr Ser Asn Leu Trp Val Val Thr 305 310 315 320

Pro Gln His Asn Met Gly Leu Gln Leu Ser Val Val Thr Arg Asp Gly 325 330 335

Val His Val His Pro Arg Ala Ala Gly Leu Val Gly Arg Asp Gly Pro 340 345 350

Tyr Asp Lys Gln Pro Phe Met Val Ala Phe Phe Lys Val Ser Glu Val 355 360 365

His Val Arg Thr Thr Arg Ser Ala Ser Ser Arg Arg Gln Gln Ser 370 380

Arg Asn Arg Ser Thr Gln Ser Gln Asp Val Ala Arg Val Ser Ser Ala 385 390 395 400

Ser Asp Tyr Asn Ser Ser Glu Leu Lys Thr Ala Cys Arg Lys His Glu 405 410 415

Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala 420 425 430

Pro Lys Gly Tyr Ala Ala Asn Tyr Cys Asp Gly Glu Cys Ser Phe Pro 435 440 445

Leu Asn Ala His Met Asn Ala Thr Asn His Ala Ile Val Gln Thr Leu 450 455 460

Val His Leu Met Asn Pro Glu Tyr Val Pro Lys Pro Cys Cys Ala Pro 465 470 475 480

Thr Lys Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asn Ser Asn 485 490 495

Val Ile Leu Lys Lys Tyr Arg Asn Met Val Val Arg Ala Cys Gly Cys 500 505 510

His

<210> 17

<211> 1822

<212> DNA

<213> Homo sapiens

<400> 17

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<210> 18 <211> 1873 <212> DNA <213> Mus musculus

<400> 18

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tcgcccgcgc	ccgcacctcc	agggaaagca	taattcggcg	cccatgttca	tgttggacct	360
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<212> PRT

<213> Mus musculus

<400> 19

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Leu Trp Ala Pro Leu Phe Leu Leu Arg Ser Ala Leu Ala Asp Phe Ser 20 25 30

Leu Asp Asn Glu Val His Ser Ser Phe Ile His Arg Arg Leu Arg Ser 35 40 45

Gln Glu Arg Arg Glu Met Gln Arg Glu Ile Leu Ser Ile Leu Gly Leu 50 55 60

Pro His Arg Pro Arg Pro His Leu Gln Gly Lys His Asn Ser Ala Pro 65 70 75 80

Met Phe Met Leu Asp Leu Tyr Asn Ala Met Ala Val Glu Glu Ser Gly 85 90 95

Pro Asp Gly Gln Gly Phe Ser Tyr Pro Tyr Lys Ala Val Phe Ser Thr 100 105 110

Gln Gly Pro Pro Leu Ala Ser Leu Gln Asp Ser His Phe Leu Thr Asp 115 120 125

Ala Asp Met Val Met Ser Phe Val Asn Leu Val Glu His Asp Lys Glu 130 135 140

Phe Phe His Pro Arg Tyr His His Arg Glu Phe Arg Phe Asp Leu Ser 145 150 155 160

Lys Ile Pro Glu Gly Glu Arg Val Thr Ala Ala Glu Phe Arg Ile Tyr 165 170 175

Lys Asp Tyr Ile Arg Glu Arg Phe Asp Asn Glu Thr Phe Gln Ile Thr 180 185 190

Val Tyr Gln Val Leu Gln Glu His Ser Gly Arg Glu Ser Asp Leu Phe 195 200 205

Phe Asp Ile Thr Ala Thr Ser Asn His Trp Val Val Asn Pro Arg His Asn Leu Gly Leu Gln Leu Ser Val Glu Thr Leu Asp Gly Gln Ser Ile Asn Pro Lys Leu Ala Gly Leu Ile Gly Arg His Gly Pro Gln Asn Lys Gln Pro Phe Met Val Ala Phe Phe Lys Ala Thr Glu Val His Leu Arq Ser Ile Arg Ser Thr Gly Gly Lys Gln Arg Ser Gln Asn Arg Ser Lys Thr Pro Lys Asn Gln Glu Ala Leu Arg Met Ala Ser Val Ala Glu Asn Ser Ser Asp Gln Arg Gln Ala Cys Lys His Glu Leu Tyr Val Ser Phe Arg Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala Pro Glu Gly Tyr Ala Ala Tyr Tyr Cys Glu Gly Glu Cys Ala Phe Pro Leu Asn Ser Tyr Met Asn Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His Phe Ile Asn Pro Asp Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp Ser Ser Asn Val Ile Leu Lys Lys Tyr Arg Asn Met Val Val Arg Ala Cys Gly Cys His

Leu Leu Asp Ser Arg Thr Ile Trp Ala Ser Glu Glu Gly Trp Leu Val

<211> 1723

<212> DNA

<213> Homo sapiens

<400> 20

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Leu Ala Val Leu Gly Leu Pro Gly Arg Pro Arg Pro Arg Ala Pro Pro 50 55 60													
Ala Ala Ser Arg Leu Pro Ala Ser Ala Pro Leu Phe Met Leu Asp Leu 65 70 75 80													
Tyr His Ala Met Ala Gly Asp Asp Asp Glu Asp Gly Ala Pro Ala Glu 85 90 95													
Arg Arg Leu Gly Arg Ala Asp Leu Val Met Ser Phe Val Asn Met Val 100 105 110													
Glu Arg Asp Arg Ala Leu Gly His Gln Glu Pro His Trp Lys Glu Phe 115 120 125													
Arg Phe Asp Leu Thr Gln Ile Pro Ala Gly Glu Ala Val Thr Ala Ala 130 135 140													
Glu Phe Arg Ile Tyr Lys Val Pro Ser Ile His Leu Leu Asn Arg Thr 145 150 155 160													
Leu His Val Ser Met Phe Gln Val Val Gln Glu Gln Ser Asn Arg Glu 165 170 175													

- Ser Asp Leu Phe Phe Leu Asp Leu Gln Thr Leu Arg Ala Gly Asp Glu 180 185 190
- Gly Trp Leu Val Leu Asp Val Thr Ala Ala Ser Asp Cys Trp Leu Leu 195 200 205
- Lys Arg His Lys Asp Leu Gly Leu Arg Leu Tyr Val Glu Thr Glu Asp 210 215 220
- Gly His Ser Val Asp Pro Gly Leu Ala Gly Leu Leu Gly Gln Arg Ala 225 230 235 240
- Pro Arg Ser Gln Gln Pro Phe Val Val Thr Phe Phe Arg Ala Ser Pro 245 250 255
- Ser Pro Ile Arg Thr Pro Arg Ala Val Arg Pro Leu Arg Arg Gln 260 265 270
- Pro Lys Lys Ser Asn Glu Leu Pro Gln Ala Asn Arg Leu Pro Gly Ile 275 280 285
- Phe Asp Asp Val His Gly Ser His Gly Arg Gln Val Cys Arg Arg His 290 295 300
- Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Leu Asp Trp Val Ile 305 310 315 320
- Ala Pro Gln Gly Tyr Ser Ala Tyr Tyr Cys Glu Gly Glu Cys Ser Phe 325 330 335
- Pro Leu Asp Ser Cys Met Asn Ala Thr Asn His Ala Ile Leu Gln Ser 340 345 350
- Leu Val His Leu Met Lys Pro Asn Ala Val Pro Lys Ala Cys Cys Ala 355 360 365
- Pro Thr Lys Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp Ser Ser Asn 370 380
- Asn Val Ile Leu Arg Lys His Arg Asn Met Val Val Lys Ala Cys Gly 385 390 395 400

<210> 22 <211> 1926 <212> DNA

<213> Mus musculus

<400> 22

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tgctcgggct	accgggacgg	ccccgacccc	gtgcacaacc	cgccgctgcc	cggcagccag	300
cgtccgcgcc	cctcttcatg	ttggacctat	accacgccat	gaccgatgac	gacgacggcg	360
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His Ala Met Thr Asp Asp Asp Gly Gly Pro Pro Gln Ala His Leu 85 90 95

Gly Arg Ala Asp Leu Val Met Ser Phe Val Asn Met Val Glu Arg Asp 100 105 110

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<223> Xaa is (Ile, Asn, Val, Leu, Tyr, Asp or Ala)
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<223> Xaa is (His, Arg, Gly, Leu or Ser)
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Xaa Xaa Xaa Xaa Pro Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Gly
                     25
50
Xaa Xaa Cys Xaa Pro Xaa Xaa Xaa Xaa Xaa Xaa Xaa Leu Xaa Xaa
                           75
                                        80
90
Xaa Xaa Cys Xaa Cys Xaa
        100
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<211> 101
<212> PRT
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<223> Xaa at res. 3 is (Lys or Arg)
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<222> (11)..(11)
<223> Xaa at res. 11 is (Arg or Gln)
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<223> Xaa at res. 16 is (Gin or Leu)
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<221>
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<223> Xaa. at res. 19 is (Ile or Val)
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<223> Xaa at res. 23 is (Glu or Gln)
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<223> Xaa at res. 26 is (Ala or Ser)
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<223> Xaa at res. 35 is (Ala or Ser)
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<223> Xaa can be any naturally occurring amino acid
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<223> Xaa at res. 41 is (Tyr or Cys)
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<223> Xaa at res. 50 is (Val or Leu)
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<223> Xaa at res. 52 is (Ser or Thr)
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<223> Xaa at res. 57 is (Ile or Met)
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<223> Xaa at res. 60 is (Glu, Asp or Asn)
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<223> Xaa at res. 61 is (Thr, Ala or Val)
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<223> Xaa at res. 65 is (Pro or Ala)
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<223> Xaa at res. 71 is (Gln or Lys)
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<223> Xaa at res. 73 is (Asn or Ser)
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<223> Xaa at res. 75 is (Ile or Thr)
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<223> Xaa at res. 80 is (Phe or Tyr)
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<223> Xaa at res. 82 is (Asp or Ser)
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<223> Xaa at res. 84 is (Ser or Asn)
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<223> Xaa at res. 89 is (Lys or Arg)
<220>
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<223> Xaa at res. 91 is (Tyr or His)
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<223> Xaa at res. 97 is (Arg or Lys)
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                                    10
Asp Trp Xaa Ile Ala Pro Xaa Gly Tyr Xaa Ala Tyr Tyr Cys Glu Gly
            20
                                25
Glu Cys Xaa Phe Pro Leu Xaa Ser Xaa Met Asn Ala Thr Asn His Ala
        35
                            40
Ile Xaa Gln Xaa Leu Val His Xaa Xaa Xaa Pro Xaa Xaa Val Pro Lys
    50
                        55
Xaa Cys Cys Ala Pro Thr Xaa Leu Xaa Ala Xaa Ser Val Leu Tyr Xaa
                    70
Asp Xaa Ser Xaa Asn Val Ile Leu Xaa Lys Lys Arg Asn Met Val Xaa
Ala Cys Gly Cys His
            100
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<212> PRT
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Arg Xaa Xaa Arg

<210> 31 <211> 4 <212> PRT <213> Artificial

<400> 31

Gly Gly Pro Pro